Remarks/Arguments

Claims 1-10 are pending in the application. Claims 1-10 are rejected.

A petition for a three (3) month extension of time is being submitted concurrently via EFS.

Claims 1-10 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claims 1 and 9 the term "through" is deemed to be vague and to render the claims indefinite. Applicant submits the term "through" is clear and definite. Nonetheless, to advance prosectution, by the present amendment claims 1 and 9 have been amended by changing the word "through" to "using" as suggested by the examiner.

Claims 1-6, 8 and 9 are rejected under 35 U.S.C. §103(a) as being unpatentable over Dick *et al.* (FR 2336931) of record in view of Lur'e *et al.* This rejection is respectfully traversed.

In the Office Action it is asserted that "Dick *et al.* teach that new pharmaceutical compositions containing mebendazole can be formulated in suspensions comprising water and can be added to an animal feed or drinking water." It is stated further on page 4 of the office action that "Dick *et al.* teach compositions comprising mebendazole, water, glycerin (water-immiscible liquid), and stabilizing agents" and on page 5 that Dick *et al.* teach the composition "comprising the same components as the composition utilized in the instant claim 1".

Applicant's invention resides in the provision of a method of preparing a veterinary composition comprising a water-insoluble active compound suitable for administering to a target animal using a water distribution system. The claimed composition is prepared by first mixing the active compound with a water-immiscible liquid (i.e. an oil such as vegetable oil) and then mixing the solid in oil suspension with water or an aqueous carrier in such a manner that the mixture of active compound and water-immiscible liquid has a density which is near to the density of water and suspending the mixture in an aqueous carrier to form an emulsion. The resulting formulation is what is known in the art as a "suspoemulsion". A suspoemulsion is a solid in oil in water emulsion system that consists of solid particles and oil droplets suspended in a continuous aqueous phase that allows delivery as a liquid bulk or packaged product. Suspoemulsions are not suspensions of a water insoluble solid in water but rather consist of three phases: a solid phase, a water immiscible liquid phase and a water phase. (See paragraph 12 on page 3 of the application where the invention is described as a solid in oil in water emulsion.) . A suspension on the other hand is a noncolloidal dispersion of solid particles in a liquid that is often used for pharmaceutical preparations.

In the Office Action it is stated that Dick *et al.* teach that new pharmaceutical compositions containing mebendazole can be formulated in suspensions comprising water. Claims 15-20 of the cited patent are drawn to aqueous suspensions. There is no description in Dick *et al.* of a solid in oil in water emulsion such as the emulsions described and claimed in the instant application. Examples I-IV, X, XI-XIII and XVII of Dick *et al.* describe compositions that are clearly suspensions and not emulsions. The remaining Examples are mostly pastes or powders. The addition of a suspension containing a solid active directly into drinking water often results in precipitation or creaming of the active ingredient in the storage vessel or in the water pipes during the 8-12 hours normally employed in drug administration through drinking water systems. In applicant's suspoemulsion, depending on the density of the active ingredient, the water immiscible liquid employed preferably has a density, which compensates for the density of the active ingredient. This leads to a combined specific density of the solid-immiscible liquid aggregate, which is more or less equal to the density of water. The claimed suspoemulsion prevents or slows down the creaming or precipitation of the active ingredient during storage and usage.

The present invention provides a formulation that can administer a water insoluble active compound through the drinking water system without causing problems such as sedimentation which often occurs with suspensions. The stability of the claimed suspoemulsions in storage and in use as well as the slow down of the precipitation or creaming of the active ingredient have been described in Example 2 of the application. Dick *et al.* and Lur'e *et al.* are silent as to the stability of the two phase suspensions described therein. The proven stability and the lack of creaming or precipitation of the active ingredient in the claimed three phase suspoemulsions of the present invention are not obvious in view of the disclosure in the references.

The Office Action states that "Dick *et al.* teaches the composition comprising [the] same components as the composition utilized in the instant claim 1". Example 6 (VI) on page 6 of Dick *et al* is relied on for support of this conclusion. The cited Example describes the preparation of a paste in a water base which contains glycerin as the wetting agent (agent mouillant). According to the Merck Index glycerol (or glycerin) is miscible with water and, therefore, is not a water-immiscible liquid. Thus Dick *et al.* does not teach a composition comprising the same components as the composition utilized in the instant claim 1. The Office Action states that Dick *et al.* do not teach the specified density and the specified ratio set forth in claims 4 and 9 or the particle size set forth in claim 8. As indicated above, the density of the solid-immiscible liquid aggregate prevents creaming or precipitation of the solid active ingredient during storage or use. The Office Action states that the density would be obvious "since they are all within the knowledge of the skilled pharmacologist and represent conventional formulations…" As indicated above on page 5, lines 25-28 of the application, the density of the water immiscible liquid has a density which compensates for the density of the active ingredient. This leads to a combined specific density of the solid-immiscible liquid aggregate that is equal to the density of water. Since the two phase compositions taught by Dick *et al.* differ from applicant's three phase solid in oil in water emulsions, contrary to the conclusion reached in the Office Action, the Dick *et al.*

compositions would not teach or suggest compositions which have the same density as the claimed compositions.

It is submitted that applicant's claimed formulations are not obvious over the disclosure in Dick *et al.* in view of Lur'e *et al.* Reconsideration of the rejection of claims 1-6, 8 and 9 under 35 U.S.C. §103(a) as being unpatentable over Dick *et al.* (FR 2336931) of record in view of Lur'e *et al.* is requested.

Claims 7 and 10 are rejected under 35 U.S.C. §103(a) as being unpatentable over Dick *et al.* of record in view of Lur'e *et al.* In addition to the disclosure in Dick *et al.*, Lur'e *et al.* is relied on in the Office Action as teaching that mebendazole can be formulated with sunflower, corn, mustard, olive or apricot oils and that sunflower oil was the most effective vehicle because it increased the bioavailability and the therapeutic levels of mebendazole in the blood of mice. Applicant submits that Lur'e *et al.* relate to the use of vegetable oils to enhance the bioavailability of mebendazole. The mebendazole was mixed with vegetable oil and left to stand for 1.5-2 hours at room temperature before administration to mice. The sunflower oil formulations were not mixed with water prior to their administration to mice. In fact, Lur'e *et al.* indicate on page 4 of the translation provided to the examiner that "More prolonged circulation of the preparation in the blood evidently led to some retention of this [preparation] in the body in deposited form". Precipitation of some of the solid ingredient from suspensions or mixtures is a common occurrence. There is nothing in Lur'e *et al.* to indicate that the mixture of mebendazole in vegetable oil would exhibit the same properties when mixed with water and administered to animals. Since the resulting formulation prepared in the manner taught by Dick *et al.* as indicated by the examiner, would be a suspension of the mebendazole, it is likely that some of the solid would precipitate as indicated in Lur'e *et al.* above. Applicant has indicated above that the glycerin employed in Dick *et al.* is not a water immiscible liquid. Therefore, it would not have been obvious to one of ordinary skill in the art to modify the mebendazole formulation of Dick *et al.* by employing sunflower oil since the mere addition of the Lur'e *et al.* formulation to the Dick *et al.* formulation would not result in the three phase solid in oil in water suspoemulsion claimed by applicant.

Applicant's claimed formulations are three phase solid in oil in water emulsions having a density between 0.85 and 1.2. All of the formulations disclosed in Dick *et al.* and Lur'e *et al.* are two phase solid in water or solid in oil suspensions. There is nothing in either reference, whether taken alone or in combination, that would render obvious applicant's three phase solid in oil in water emulsions. Accordingly, applicant requests that the rejection under 35 U.S.C. §103(a) be withdrawn.

Applicants respectfully request that a timely Notice of Allowance be issued in this case.

Respectfully submitted,

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